HELSINGIN YLIOPISTO — HELSINFORS UNIVERSITET

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Tekijä – Författare
Aino KIRSTI Hillevi Torniainen

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Photodegradation of Ciprofloxacin in Aqueous Solutions

Oppiaine – Läroämne
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Ciprofloxacin is a synthetic broad-spectrum fluoroquinolone antibiotic structurally related to nalidixic acid. As an amphoteric compound, it contains a carboxylic group in 3-position of the quinoline ring-structure and a *secondary* amino group in the piperazinyl side-chain. Ciprofloxacin is present in commercially available liquid dosage forms as lactate or hydrochloride salt.

It has long been recognized that fluoroquinolones, and all their structural analogues, are both phototoxic and photosensitive, yet there are very few publications dealing with the photodegradation of these compounds.

In this study the photochemical degradation of ciprofloxacin was investigated in aqueous solutions exposed to a high-pressure mercury lamp and daylight. A thin layer chromatographic method (TLC) was developed, primarily for qualitative monitoring of the photochemical degradation, while horizontal high-performance thin layer chromatography (HPTLC) with subsequent densitometric measurement was applied for quantitative analyses. An isocratic reversed-phase ion-pair high-performance liquid chromatographic (RP-HPLC) method was developed for more detailed monitoring of the photochemical degradation of ciprofloxacin in aqueous solutions.

Formation of photodegradation products in the solutions exposed to light depended on the pH, with the number of the products increasing with pH. The two main decomposition products formed in acidic solutions were isolated by flash chromatography or by precipitation, and the structures were elucidated by UV, IR, MS and NMR methods. The final assignment of the protons and carbons in the NMR spectra was performed by two-dimensional NMR techniques: COSY, HMQC and HMBC. The only photochemical changes observed were in the piperazine ring of ciprofloxacin, which was partially cleaved off and finally replaced by an amino group. The degradation products were identified as 7[(2-aminoethyl)amino]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline carboxylic acid and 7-amino-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline carboxylic acid. The former compound seemed to be an intermediate, which upon longer exposure to irradiation degraded further to the aromatic amine.

The photodegradation rate of ciprofloxacin was studied at wavelength 313 nm, which was isolated from the mercury lamp with a potassium chromate filter solution in combination with a Corning filter plate. Tap water was used to cool the glass cuvettes. Irradiation intensity of the lamp and the quantum yields of the photodegradation reactions were measured and calculated by ferrioxalate chemical actinometry. Under all conditions studied, the disappearance of ciprofloxacin followed approximate first-order kinetics. The reaction rate was inversely proportional to the initial drug concentration. Similar concentration-dependence of photodegradation was detected in solutions after exposure to daylight. Ciprofloxacin was most unstable in zwitterionic form in pH range 6 to 9 and the stability increased considerably at lower pH. The type of buffer species had no substantial influence on the degradation.

In commercial liquid pharmaceutical formulations of ciprofloxacin, the pH is acidic and the concentration level so high that special arrangements for light-protection in the administration of these dosage forms seem unnecessary, but protection from light during storage is recommended. In clinical samples, the concentration level is low and the pH often near neutral, and light-protective sample treatment is required.

Avainsanat – Nyckelord
ciprofloxacin, photodegradation, high perfomance liquid chromatograph

Säilytyspaikka – Förvaringställe
Farmasian laitos, farmaseuttisen kemian osasto

Muita tietoja – Övriga uppgifter